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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/031,844	07/17/2002	David Thomas Davies	P32372	8478

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EXAMINER	
BALASUBRAMANIAN, VENKATARAMAN	
ART UNIT	**PAPER NUMBER**
1624	

DATE MAILED: 12/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/031,844	DAVIES ET AL.	
	Examiner	Art Unit	
	Venkataraman Balasubramanian	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 11-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 11-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3,10*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicant's election with traverse of Group III, claims 1-2, 11-18, wherein one of Z^1, Z^2, Z^3 is nitrogen and the other along with Z^4, Z^5 are CR^{1a}, in Paper No. 9 is acknowledged. Claims 1-2 and 11-18 will be examined to the extent they embrace the elected subject matter.

Applicant is reminded again that upon the cancellation of claims to a non-elected subject matter, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

The traversal is on the ground(s) that the inventions as grouped by the examiner are not independent but patentably distinct and that the bicyclic aromatic ring and piperidine ring are essential for the utility. This is not found persuasive because for reasons of record. As for the traversal, the following apply:

The requirement for unity of invention is two-fold: (1) common utility and (2) sharing a substantial structural feature disclosed as being essential to the utility. Both these conditions are to be met with.

In the instant case, both these conditions are not met with.

1. First of all applicants argue that the inventions as grouped by the examiner are not independent but have not provided any evidence or reason why they are not independent. Instead applicants admit they are patentably distinct but offer no

reasons as to why compounds with different structural cores to be held as not independent but distinct. As noted in the previous office action examiner had given reasons why they are independent and distinct. Hence, the first criteria of unity of invention is lacking.

2. Secondly, applicants' argument that the bicyclic aromatic ring and piperidine ring are essential for the utility lacks factual support. First of all, applicants have not provided any evidence or teaching in the specification that any bicyclic heterocore as embraced in the instant invention share the same utility. In addition, several references cited in the information disclosure statement teach that the biccylic aromatic core along with a piperidine have variety of pharmacological activity including cardiovascular, antipscyhotic and cognitive activity. See BE 706646, NL 7908030, EP 296 560, EP 0 579 263 etc. Thus there is no evidence that the combination of bicyclic aromatic and piperidine core is essential for utility. Thus the common utility criterion is also lacking.

Hence both the criteria of unity of invention are lacking.

The requirement is still deemed proper and is therefore made FINAL.

Information Disclosure Statement

References cited in the Information Disclosure Statements (paper# 3 and 10) are made of record.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-2 and 11-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Following reasons apply. Any claim not specifically rejected is rejected as being dependent on a rejected claim.

1. Claim 1 is indefinite as formula I is unclear as to the substituent at the 4- position of the piperidine ring. Note the substitutents is shown as $(NR^2)R^4$ and as recited it appears that R^4 is attached directly to the 4-position of the piperidine ring in which case the valence requirement of nitrogen shown in the parenthesis is not met with. If R^4 is meant to be attached to the nitrogen, then the need for the parenthesis is unclear.

2. Recitation of "derivative" in the claims 1 and 17-18, renders these claims indefinite as term " derivative" can include more than what is being positively recited therein. Note the term "derivative' can be any organic group with elected core and hence the structural make-up of the compounds embraced remains unknown.

3. Also in claim1, the recitation of the group $CH(R^{13})CO_2NH_2$ appears to be typographical error. Note "CO_2" would imply attachment of NH_2 to oxygen not carbon as normally expected for natural α-amino acid.

4. Also in line 25 of claim 1, the phrase "optionally further substituted..." which follows $CH(R^{13})CO_2NH_2$ is unclear as to which group is to be further substituted. This is true for number of varible definitions in claim 1. An appropriate correction is needed.

5. The proviso on line 30 of claim 1 is no longer applicable in view of applicants' election.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 18 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating bacterial infections due to S. aureus and S. pneumoniae does not reasonably provide enablement for any or all bacterial infections The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Following reasons apply.

The instant claim 18 is drawn to "treating any or all bacterial infection The scope of the claims includes not only include treating any or all bacterial infections which is not adequately enabled solely based on the activity of the compounds provided in the specification at page 31. The instant compounds are disclosed to have bacterial inhibitory activity and it is recited that the instant compounds are useful in treating bacterial infection, for which applicants provide no competent evidence. The fact that a single class of compounds can be used treat any or all bacterial infections is new finding for which there is no support in the prior art. Note substantiation of utility and its scope is required when utility is "speculative", "sufficiently unusual" or not provided. See Ex parte Jovanovics, 211 USPQ 907, 909; In re Langer 183 USPQ 288. Also note Hoffman v. Klaus 9 USPQ 2d 1657 and Ex parte Powers 220 USPQ 925 regarding type of testing

needed to support in vivo uses. Next, applicant's attention is drawn to the Revised Interim Utility and Written Description Guidelines, at 64 FR 71427 and 71440 (December 21, 1999) wherein it is emphasized that 'a claimed invention must have a specific and substantial utility'. The disclosure in the instant case is not sufficient to enable the instantly claimed treating of any or bacterial infections solely based on the inhibitory activity disclosed for the compounds. The state of the art is indicative of the requirement for undue experimentation. See Snyder et al., J. Med. Liban 48(4): 208-214, 2000 (PubMed Abstract provided), wherein with regards to antibacterial therapies, it is stated that " common bacteria whose susceptibility to antimicrobials is no longer predictable". Note also that despite the fact there are several commercial antibacterial agents are available, it is still difficult to treat several pathogens such as those cause leprosy, meningitis, sexually transmitted infections, anthrax etc.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1) The nature of the invention: Therapeutic use of the compounds in treating bacterial infections.

2) The state of the prior art: A very recent publication expressed that the antibacterial effects of bacterial inhibitors are unpredictable.

3) The predictability or lack thereof in the art: Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use for treating any or all condition of the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

4) The amount of direction or guidance present and 5) the presence or absence of working examples: Specification has no working examples to show treating any or all bacterial infection and the state of the art is that the effects of bacterial inhibitors are unpredictable.

6) The breadth of the claims: The instant claims embrace not only treatment of bacterial infections

7) The quantity of experimentation needed would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan, regarding the pharmaceutical use, for the reasons stated above.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims. In view of the breadth of the claims, the chemical nature of the invention, the unpredictability of enzyme-inhibitor interactions in general, and the lack of working examples regarding the activity of the claimed compounds towards treating the variety of bacterial infections of the instant claims, one having

ordinary skill in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

Allowable Subject Matter

Claims 1-2 and 11-17 would be allowable, barring finding of any prior art in a subsequent search, if rewritten or amended to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action. Said claims would be allowed since specific species and composition embraced in these claims are not taught or suggested by the art of record or from a search in the relevant art area.

Conclusion

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (703) 305-1674. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is Mukund Shah whose telephone number is (703) 308-4716. The fax phone number for the organization where this application or proceeding is assigned (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

V. Balasubramanian
Venkataraman Balasubramanian

12/22/2003